

CLAIMS

1. A gene therapy vector, comprising:
 - a first polynucleotide encoding a gene for β subunit of a cytolethal distending toxin; and
 - a second polynucleotide encoding an antisense oligonucleotide that inhibits expression of a sense oligonucleotide encoding a DNA repair protein;
 - wherein the first and second polynucleotides are operably linked to an inducible promoter.
2. The gene therapy vector of claim 1, wherein the inducible promoter is a heat shock promoter.
3. The gene therapy vector of claim 1, wherein the inducible promoter is a segment of a heat shock promoter that is strictly inducible by heat shock.
4. The gene therapy vector of claim 3, wherein the inducible promoter has nucleotide sequence SEQ ID 7.
5. The gene therapy vector of claim 1, wherein the gene is selected from the group consisting of *H. ducreyi* cdtB, *C. jejuni* cdtB, and *E.coli* cdtB.
6. The gene therapy vector of claim 1, wherein the gene is *E.coli* cdtB.

7. The gene therapy vector of claim 6, wherein the gene has nucleotide sequence SEQ ID 5.

8. The gene therapy vector of claim 1, wherein the second polynucleotide encodes an antisense oligonucleotide that inhibits expression of a sense oligonucleotide encoding a protein involved in the non-homologous end-joining DNA repair mechanism.

9. The gene therapy vector of claim 8, wherein the protein is ku70.

10. The gene therapy vector of claim 9, wherein the second polynucleotide is complimentary to nucleotide sequence SEQ ID 6.

11. The gene therapy vector of claim 1, wherein the vector is a member selected from the group consisting of plasmids, phages, phagemids, viruses, and artificial chromosomes.

12. The gene therapy vector of claim 11, wherein the vector is a viral vector.

13. The gene therapy vector of claim 12, wherein the vector is a member selected from the group consisting of papovirus, lentivirus, adenovirus, vaccinia virus, adeno-associated virus, herpes virus, and retrovirus.

14. An adenoviral vector for performing cytolethal gene therapy, comprising a polynucleotide having a first nucleotide sequence encoding a cdtB gene, a second nucleotide sequence encoding an antisense oligonucleotide that inhibits expression of ku70, and a heat shock promoter that is strictly inducible by heat and is positioned to promote expression of the first and second nucleotide sequences.

15. The adenoviral vector of claim 14, wherein the cdtB gene has nucleotide sequence SEQ ID 5.

16. The adenoviral vector of claim 14, wherein the second nucleotide sequence is complimentary to nucleotide sequence SEQ ID 6.

17. The adenoviral vector of claim 14, wherein the heat shock promoter has nucleotide sequence SEQ ID 7.

18. A method of conducting cytolethal gene therapy, comprising:
providing a vector comprising a first polynucleotide encoding a gene for a B subunit of a cytolethal distending toxin, a second polynucleotide encoding an antisense oligonucleotide that inhibits expression of a sense oligonucleotide encoding a DNA repair protein, and a heat shock promoter operably linked to the first and second polynucleotides;
delivering the vector to a desired cell; and

elevating the temperature of the cell above normal body temperature such that the promoter transcribes the first and second polynucleotides.

19. The method of claim 18, wherein the heat shock promoter is a segment of a heat shock promoter that is strictly inducible by heat shock.

20. The method of claim 19, wherein the heat shock promoter has nucleotide sequence SEQ ID 7.

21. The method of claim 20, wherein the gene is *E.coli* cdtB.

22. The method of claim 21, wherein the gene has nucleotide sequence SEQ ID 5.

23. The method of claim 21, wherein the vector is a viral vector.

24. The method of claim 23, wherein the vector is a member selected from the group consisting of papovirus, lentivirus, adenovirus, vaccinia virus, adeno-associated virus, herpes virus, and retrovirus.

25. The method of claim 18, wherein delivering the vector comprises directly infusing the vector into a tissue comprising the cell.

26. The method of claim 18, wherein the cell is a cancerous cell.

27. The method of claim 26, wherein the cancerous cell is contained within a solid tumor.

28. The method of claim 18, wherein elevating the temperature of the cell comprises elevating the temperature of the cell to a temperature between approximately 38 and 45° C.

29. The method of claim 28, wherein the elevated temperature is approximately 41°C.

30. The method of claim 30, further comprising maintaining the elevated temperature of the cell for between approximately 1 and 72 hours.

31. A method of conducting cytolethal gene therapy, in a tumor, comprising:

delivering to said tumor a polynucleotide encoding a cdtB gene, an antisense oligonucleotide that inhibits expression of ku70, and a heat shock promoter that is strictly inducible by heat and is positioned to promote expression of the cdt β gene and the antisense oligonucleotide; and

elevating the temperature of said tumor.